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DOCKET NO. JAB1703USPCT

85
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Anne Simone Josephine Lesage et al.

Serial No.: 10/509,069

Art Unit:

I.A. Filing Date: March 26, 2003

Examiner:

For : RADIOLABELLED QUINOLINE AND QUINOLINONE DERIVATIVES AND
THEIR USE AS METABOTROPIC GLUTAMATE RECEPTOR LIGANDS

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Missing Parts, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

November 18, 2005

(Date of Deposit)

Hal B. Woodrow

(Name of applicant, assignee, or Registered Representative)

/Hal Brent Woodrow, Reg. # 32,501/

(Signature)

November 18, 2005

(Date of Signature)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NOTIFICATION TO COMPLY WITH REQUIREMENTS
FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE
AND/OR AMINO ACID SEQUENCE DISCLOSURES

Dear Sir:

Applicant's attorney is in receipt of the Notification To Comply With Requirements For Patent Applications Containing Nucleotide And/Or Amino Acid Sequence Disclosures.

With respect to defects in the previously submitted Preliminary Amendment, applicant has now corrected said defects and now submits a revised Preliminary Amendment for entry.

With respect to the requirement for submission of a sequence listing, applicant's attorney has reviewed the above-identified patent

application and has not found any nucleic acid or amino acid sequences that would require a sequence listing.

The abbreviations on page 108 of the specification are for compounds only. For the Examiner's convenience, applicant is attaching copies of webpages from the Tocris Bioscience website and the Perkin Elmer website listing the full names of the compounds listed on page 108 of the specification.

Accordingly, applicant's attorney respectfully requests withdrawal of the requirement to provide a sequence listing for this application.

In addition, applicant does not believe that any extension fees or other patent fees are due at this time since the Notification to Comply was issued in error. If, however, the Patent Office does deem any fee necessary at this time, the Commissioner is then hereby authorized to charge said required fee to Deposit Account No. 10-0750/JAB1703USPCT/HBW. This sheet is submitted in triplicate.

Respectfully submitted,

/Hal Brent Woodrow/
Hal B. Woodrow
Reg. No. 32,501
Attorney for Applicant(s)

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-2976

Void date: 12/29/2005 BCAMPBEL
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U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/509,069	Anne Simone Josephine Lesage	JAB-1703

INTERNATIONAL APPLICATION NO.

PCT/EP03/03240

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03/26/2003	03/29/2002

CONFIRMATION NO. 3249

J&I PAT. DKT. SECTION 371 FORMALITIES LETTER



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Date Mailed: 06/24/2005

NOTIFICATION TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to file the items indicated below to avoid abandonment. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c) Applicant must provide an initial paper or compact disc copy of the "Sequence Listing", as well as an amendment directing its entry into the application and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000).
- A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e). If the effective filing date is on or after September 8, 2000, see the final rulemaking notice published in the Federal Register at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the U.S. Patent and Trademark Office, such request in accordance with 37 CFR 1.821(e) may be submitted in lieu of a new CRF.

Additionally the following defects have been observed:

- Preliminary Amendments have not been entered because Original application consists of claims 1-20. Preliminary Amendment addresses only claims 1-17. Please clarify the status of claims 18-20..

For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.

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- Send e-mail correspondence for Patent Software Program Help @ ebc@uspto.gov

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

BARBARA A CAMPBELL

Telephone: (703) 308-9140 EXT 217

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/509,069	PCT/EP03/03240	JAB-1703

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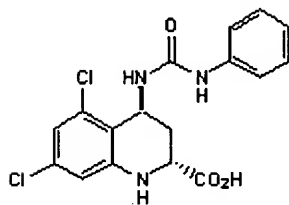
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Product/Material Safety Data Sheet:[View current batch](#)For specific/earlier batch please select: View related products by [Pharmacological Action](#) or by [Research Area](#)**Biological Activity:**

Very potent antagonist at the glycine-NMDA site.

References:

Leeson et al (1991) *trans*-2-Carboxy-4-substituted tetrahydroquinolines. Potent glycine-site NMDA receptor antagonists. *Med.Chem.Res.* **1** 64. **Leeson et al (1992)** 4-Amido-2-carboxytetrahydroquinolines. Structure-activity relationship for antagonism at the glycine site of the NMDA receptor. *J.Med.Chem.* **35** 1954. **Stone (2000)** Development and therapeutic potential of kynurenic acid and kynurenine derivatives for neuroprotection. *TIPS* **21** 149.

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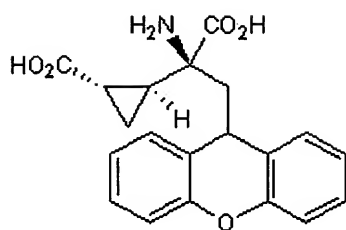
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Highly potent and selective group II metabotropic glutamate receptor antagonist (K_i/IC_{50} values are 2.3, 1.3, 173, 990, 6800, 8200 and 22000 nM for human mGlu₂, mGlu₃, mGlu₆, mGlu_{7a}, mGlu_{1a}, mGlu_{5a} and mGlu_{4a} receptors respectively). Readily brain penetrant and active in vivo.

References:

Ornstein et al (1998) 2-Substituted (2SR)-2-amino-2-((1SR,2SR)-2-carboxycycloprop-1-yl) glycines as potent and selective antagonists of group II metabotropic glutamate receptors. 2. Effects of aromatic substitution, pharmacological characterization, and bioavailability. *J. Med. Chem.* **41** 358. **Kingston et al (1998)** LY341495 is a nanomolar potent and selective antagonist of group II metabotropic glutamate receptors. *Neuropharmacology* **37** 1. **Fitzjohn et al (1998)** The potent mGlu receptor antagonist LY341495 identifies roles for both cloned and novel mGlu receptors in hippocampal synaptic plasticity. *Neuropharmacology* **37** 1445. **Johnson et al (1999)** [³H]-LY341495 as a novel antagonist radioligand for group II metabotropic glutamate receptors: characterization of binding to membranes of mGlu receptor subtype expressing cells. *Neuropharmacology* **38** 1519.

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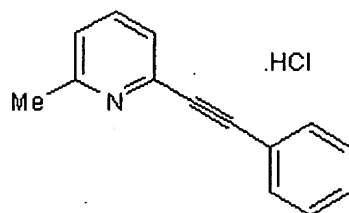
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Potent and highly selective non-competitive antagonist at the mGlu₅ receptor subtype (IC_{50} = 36 nM).

Centrally active following systemic administration in vivo.

References:

Bowes et al (1999) Anti-hyperalgesic effects of the novel metabotropic glutamate receptor 5 antagonist, methylphenylethynylpyridine, in rat models of inflammatory pain. *Br.J.Pharmacol.* **126** 250P. **Salt et al (1999)** Antagonism of the mGlu₅ agonist 2-chloro-5-hydroxyphenylglycine by the novel selective mGlu₅ antagonist 6-methyl-2-(phenylethynyl)-pyridine (MPEP) in the thalamus. *Br.J.Pharmacol.* **127** 1057. **Gasparini et al (1999)** 2-Methyl-6-(phenylethynyl)-pyridine (MPEP), a potent, selective and systemically active mGlu₅ receptor antagonist. *Neuropharmacology* **38** 1493. **Malherbe et al (2003)** Mutational analysis and molecular modeling of the binding pocket of the metabotropic glutamate 5 receptor negative modulator 2-methyl-6-(phenylethynyl)-pyridine. *Mol.Pharmacol.* **64** 823.

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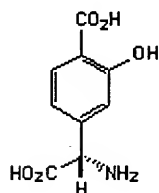
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[Home](#)[Products](#)[Shop Online](#)[Technical Support](#)[Customer Support](#)**0320** (S)-4-Carboxy-3-hydroxyphenylglycine

Alternative name(s):

(S)-4C3HPG

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Competitive antagonist at group I mGlu_{1a/1a} receptors, mixed effect at mGlu_{5a/5b} receptors; agonist at group II metabotropic glutamate receptors.

References:

Birse et al (1993) Phenylglycine derivatives as new pharmacological tools for investigating the role of metabotropic glutamate receptors in the central nervous system. *Neuroscience* **52** 481. **Hayashi et al (1994)** Analysis of agonist and antagonist activities of phenylglycine derivatives for different cloned metabotropic glutamate receptor subtypes. *J. Neurosci.* **14** 3370. **Kingston et al (1995)** Pharmacological analysis of 4-carboxyphenylglycine derivatives: comparison of effects mGluR1 α and mGluR5a subtypes. *Neuropharmacology* **34** 887. **Sekiyama et al (1996)** Structure-activity relationships of new agonists and antagonists of different metabotropic glutamate receptor subtypes. *Br.J.Pharmacol.* **117** 1493.

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[Home](#)[Products](#)[Shop Online](#)[Technical Support](#)[Customer Support](#)**0284** (1S,3R)-ACPD**Technical Data:**[Certificate of Analysis:](#)[View current batch](#)

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Active isomer of (±)-trans-ACPD.
Active at both group I and II mGlu receptors.

References:

Irving et al (1990) 1S,3R-ACPD stimulates and L-AP3 blocks Ca^{2+} mobilization in rat cerebellar neurons. *Eur.J.Pharmacol.* **186** 363. **Pin and Duvoisin (1995)** The metabotropic glutamate receptors: structure and functions. *Neuropharmacology* **34** 1. **Knopfel et al (1995)** Metabotropic glutamate receptors: novel targets for drug development. *J.Med.Chem.* **38** 1417. **Mistry and Challiss (1996)** Differences in agonist and antagonist activities for two indices of metabotropic glutamate receptor-stimulated phosphoinositide turnover. *Br.J.Pharmacol.* **117** 1735.

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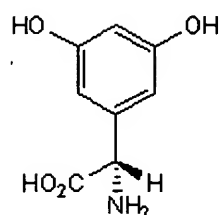
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Schoepp et al (1994) 3,5-Dihydroxyphenylglycine is a highly selective agonist for phosphoinositide-linked metabotropic glutamate receptors in the rat hippocampus. *J. Neurochem.* **63** 769.

Baker et al (1995) Enzymatic resolution and pharmacological activity of the enantiomers of 3,5-dihydroxyphenylglycine, a metabotropic glutamate receptor agonist. *Bioorg. Med. Chem. Lett.* **5** 223.

Sekiyama et al (1996) Structure-activity relationships of new agonists and antagonists of different metabotropic glutamate receptor subtypes. *Br. J. Pharmacol.* **117** 1493.

Wisniewski and Carr (2002) (S)-3,5-DHPG: a review. *CNS Drug Rev.* **8** 101.

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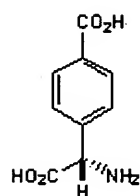
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Competitive group I metabotropic glutamate receptor antagonist, with selectivity for mGlu_{1a/1a} over mGlu_{5a/5b}.

References:

Birse et al (1993) Phenylglycine derivatives as new pharmacological tools for investigating the role of metabotropic glutamate receptors in the central nervous system. *Neuroscience* **52** 481. **Eaton et al (1993)** Competitive antagonism at metabotropic glutamate receptors by (S)-4-carboxyphenylglycine (CPG) and (RS)- α -methyl-4-carboxyphenylglycine (MCPG). *Eur.J.Pharmacol.Mol.Pharmacol.Sect.* **244** 195. **Brabet et al (1995)** Phenylglycine derivatives discriminate between mGluR1- and mGluR5-mediated responses. *Neuropharmacology* **34** 895. **Doherty et al (1999)** Antagonist activity of α -substituted 4-carboxyphenylglycine analogues at group I metabotropic glutamate receptors expressed in CHO cells. *Br.J.Pharmacol.* **126** 205.

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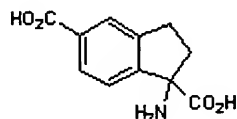
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Alternative name(s):

UPF 523

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A relatively potent and selective antagonist of group I metabotropic glutamate receptors (mGlu_{1a}), having no effect on group II (mGlu₂) or group III (mGlu₄) receptors expressed individually in baby hamster kidney cells. Has no effect on ionotropic glutamate receptors. Centrally active following systemic administration in vivo.

References:

Pellicciari et al (1995) 1-Aminoindan-1,5-dicarboxylic acid: a novel antagonist at phospholipase C-linked metabotropic glutamate receptors. *J. Med. Chem.* **38** 3717.
Nielsen et al (1997) Class I mGlu receptor antagonist 1-aminoindan-1,5-dicarboxylic acid blocks contextual but not cue conditioning in rats. *Eur. J. Pharmacol.* **326** 105.
Moroni et al (1997) Pharmacological characterization of 1-aminoindan-1,5-dicarboxylic acid, a potent mGluR1 antagonist. *J. Pharmacol. Exp. Ther.* **281** 721

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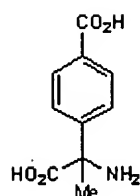
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Non-selective group I/group II metabotropic glutamate receptor antagonist. See (S)-isomer (Cat. No. 0337).

References:

Eaton et al (1993) Competitive antagonism at metabotropic glutamate receptors by (S)-4-carboxyphenylglycine (CPG) and (RS)- α -methyl-4-carboxyphenylglycine (MCPG). *Eur. J. Pharmacol. Mol. Pharmacol. Sect.* **244** 195. **Collingridge and Watkins (1994)** Phenylglycine derivatives as metabotropic glutamate receptor antagonists. *TIPS* **15** 333. **Joly et al (1995)** Molecular, functional and pharmacological characterization of the metabotropic glutamate receptor Type 5 splice variants: comparison with mGluR1. *J. Neurosci.* **15** 3970.

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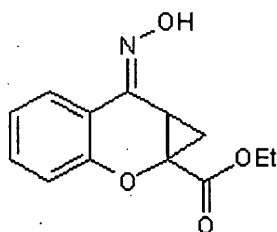
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hmGlu₁ subtype selective non-competitive antagonist (IC₅₀ = 6.5 μ M). Has no agonist or antagonist activity at hmGlu₂, 4a, 5a, 7b, 8a or ionotropic receptors at concentrations of up to 100 μ M.

References:

Annoura et al (1996) A novel class of antagonists for metabotropic glutamate receptors, 7-(hydroxyimino)cyclopropa[b]chromen-1a-carboxylates. *Bioorg. Med. Chem. Lett.* **6** 763. **Hermans et al (1998)** Reversible and non-competitive antagonist profile of CPCCOEt at the human type 1 α metabotropic glutamate receptor. *Neuropharmacology* **37** 1645. **Litschig et al (1999)** CPCCOEt, a noncompetitive metabotropic glutamate receptor 1 antagonist, inhibits receptor signaling without affecting glutamate binding. *Mol. Pharmacol.* **55** 453.

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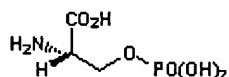
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Alternative name(s):

L-SOP

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References:

Eriksen and Thomsen (1995) [³H]-L-2-amino-4-phosphonobutyrate labels a metabotropic glutamate receptor, mGluR4a. *Br.J.Pharmacol.* **116** 3279.

Bruno et al (1996) Activation of group III metabotropic glutamate receptors is neuroprotective in cortical cultures. *Eur.J.Pharmacol.* **310** 61.

Thoreson and Ulphani (1995) Pharmacology of selective and non-selective metabotropic glutamate receptor agonists at L-AP4 receptors in ON bipolar cells. *Brain Res.* **676** 93.

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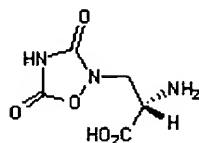
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